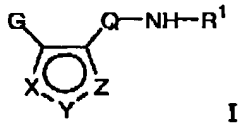
Atty. Docket No.: VPI/99-109 DIV US
Application No.: 10/779,532
Applicants: Green et al.

IN THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

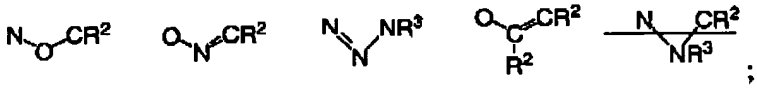
1. (Currently amended) A compound having the formula



I

wherein:

X-Y-Z is selected from one of the following:



;

R^1 is H, $CONH_2$, $T_{(n)}$-R, or $T_{(n)}$-Ar^2;

R is an aliphatic or substituted aliphatic group;

n is zero or one;

T is C(=O), CO_2, CONH, $S(O)_2$, $S(O)_2NH$, $COCH_2$ or CH_2;

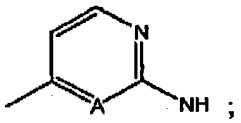
each R^2 is independently selected from hydrogen, -R, $-CH_2OR$, $-CH_2OH$, -CH=O, $-CH_2SR$, $-CH_2S(O)_2R$, $-CH_2(C=O)R$, $-CH_2CO_2R$, $-CH_2CO_2H$, $-CH_2CN$, $-CH_2NHR$, $-CH_2N(R)_2$, -CH=N-OR, -CH=NNHR, $-CH=NN(R)_2$, -CH=NNHCOR, $-CH=NNHCO_2R$, $-CH=NNHSO_2R$, -aryl, -substituted aryl, $-CH_2$(aryl), $-CH_2$(substituted aryl), $-CH_2NH_2$, $-CH_2NHCOR$, $-CH_2NHCONHR$, $-CH_2NHCON(R)_2$, $-CH_2NRCOR$, $-CH_2NHCO_2R$, $-CH_2CONHR$, $-CH_2CON(R)_2$, $-CH_2SO_2NH_2$, $-CH_2$(heterocyclyl), $-CH_2$(substituted heterocyclyl), -(heterocyclyl), or -(substituted heterocyclyl);

each R^3 is independently selected from hydrogen, R, COR, CO_2R or $S(O)_2R$;

G is R or Ar^1;

Ar^1 is aryl, substituted aryl, aralkyl, substituted aralkyl, heterocyclyl, or substituted heterocyclyl, wherein Ar^1 is optionally fused to a partially unsaturated or fully unsaturated five to seven membered ring containing zero to three heteroatoms;

Q-NH is



wherein the H of Q-NH is optionally replaced by R^3;

A is CR^3;

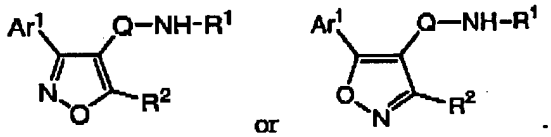
Ar^2 is aryl, substituted aryl, heterocyclyl or substituted heterocyclyl, wherein Ar^2 is optionally fused to a partially unsaturated or fully unsaturated five to seven membered ring containing zero to three heteroatoms;

wherein each substitutable carbon atom in Ar^2, including the fused ring when present, is optionally and independently substituted by halo, R, OR, SR, OH, NO_2, CN, NH_2, NHR, $N(R)_2$, NHCOR, NHCONHR, $NHCON(R)_2$, NRCOR, $NHCO_2R$, CO_2R, CO_2H, COR, CONHR, $CON(R)_2$, $S(O)_2R$, $SONH_2$, S(O)R, SO_2NHR, or $NHS(O)_2R$, and wherein each saturated carbon in the fused ring is further optionally and independently substituted by =O, =S, =NNHR, $=NNR_2$, =N-OR, =NNHCOR, $=NNHCO_2R$, $=NNHSO_2R$, or =NR; and

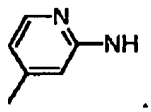
wherein each substitutable nitrogen atom in Ar^2 is optionally substituted by R, COR, $S(O)_2R$, or CO_2R.

2. (Original) The compound of claim 1 where G is Ar^1.

3. (Original) The compound of claim 2 having the formula



4. (Previously presented) The compound of claim 3 where Q-NH is

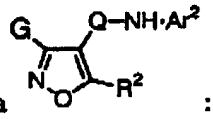


5. (Original) The compound of claim 4 where R^1 is alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, pyridinylalkyl, alkoxycycloalkyl, cycloalkyl, alkoxycarbonylcycloalkyl, hydroxycycloalkyl, Ar^2 or T-Ar^2 where T is C(=O).

6. (Original) The compound of claim 5 where R^1 is cyclohexyl, cyclohexanol-4-yl, cyclohexanon-4-yl, 2-propan-1-ol, 2-methoxy-1-methylethyl, 3-butyryl alkyl ester, 2-pyridinyl-2-ethyl, or an optionally substituted phenyl, naphthyl, pyridyl, quinolinyl, thienyl or indanyl.

7. (Original) The compound of claim 6 where R^2 is an optionally substituted alkyl.

8. (Previously presented) A compound selected from the group consisting of

(a) a compound of formula  :

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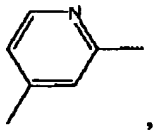
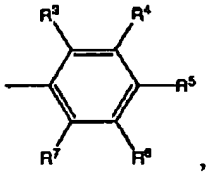
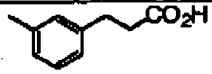
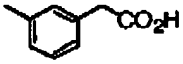
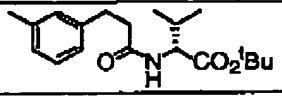
wherein Q is  ,

Ar^2 is R^1,

R^1 is  , and

G, R^2, R^3, R^4, R^5, R^6 and R^7 are defined as

No.	G	R^2	R^3	R^4	R^5	R^6	R^7
IIA-16	Phenyl	Et	H	CN	H	H	H
IIA-17	Phenyl	Et	H	CO_2H	H	H	H
IIA-18	Phenyl	Me	H	F	H	H	H
IIA-19	Phenyl	Me	H	H	F	H	H
IIA-20	Phenyl	Me	H	H	COMe	H	H
IIA-21	Phenyl	Me	H	H	COPh	H	H
IIA-24	Phenyl	Me	H	H	$CONH_2$	H	H
IIA-40	Phenyl	Et	H	H	H	H	H
IIA-43	Phenyl	Me	H	CO_2H	H	H	H
IIA-47	Phenyl	Me	H	H	OMe	H	H
IIA-48	Phenyl	Me	H	OMe	H	H	H
IIA-50	Phenyl	Me	H	CO_2Me	H	H	H
IIA-52	Phenyl	Me	H	H	H	H	H
IIA-64	Phenyl	Me	H	H	CO_2Me	H	H
IIA-67	Phenyl	Me	H	CN	H	H	H
IIA-68	Phenyl	Me	H	H	CN	H	H
IIA-98	Phenyl	Me	H	H	NMe_2	H	H
IIA-99	Phenyl	Me	H	NO_2	H	H	H
IIA-100	Phenyl	Me	H	NHAc	H	H	H
IIA-101	Phenyl	Me	H	NH_2	H	H	H
IIA-132	Phenyl	Me					
IIA-133	Phenyl	Me					
IIA-134	Phenyl	Me	H	CH_2OH	H	H	H
IIA-135	Phenyl	Me					

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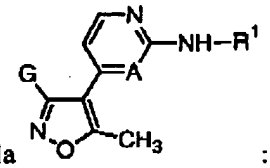
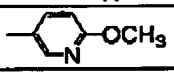
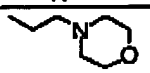
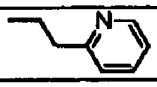
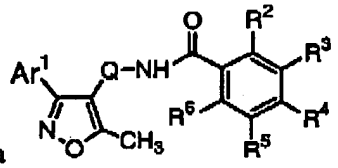
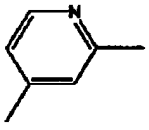
(b) a compound of formula  :

wherein G, A and R^1 are defined as

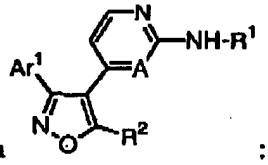
No.	G	A	R^1
IIAA-1	Phenyl	CH	
IIAA-2	Phenyl	CH	
IIAA-39	Phenyl	CH	
IIAA-40	Phenyl	CH	

(c) a compound of formula  :

wherein Q is  and

Ar^1, R^2, R^3, R^4, R^5 and R^6 are defined as

No.	Ar^1	R^2	R^3	R^4	R^5	R^6
IIIA-77	phenyl	H	COMe	H	H	H
IIIA-78	phenyl	H	CN	H	H	H

(d) a compound of formula  :

wherein Ar^1, A, R^1 and R^2 are defined as

No.	Ar^1	A	R^1	R^2
XIA-1	phenyl	CH	phenyl	CH_2(morpholin-4-yl)
XIA-2	phenyl	CH	phenyl	$CH_2N(CH_3)_2$
XIA-3	phenyl	CH	phenyl	CH_2NEt_2
XIA-4	phenyl	CH	phenyl	$CH_2N(CH_3)CH_2Ph$
XIA-5	phenyl	CH	phenyl	CH_2(1-t-butoxycarbonylpiperazin-4-yl)
XIA-6	phenyl	CH	benzyl	CH_2(morpholin-4-yl)
XIA-7	phenyl	CH	cyclohexyl	CH_2(morpholin-4-yl)
XIA-8	phenyl	CH	4-[1,2-$(OMe)_2$-phenyl]	CH_2(morpholin-4-yl)
XIA-9	phenyl	CH	4-cyclohexanol	CH_2(morpholin-4-yl)
XIA-10	phenyl	CH	phenyl	$CH_2N(CH_3)CH_2CH_2N(CH_3)_2$
XIA-11	phenyl	CH	phenyl	$CH_2N(CH_3)CH_2CO_2CH_3$
XIA-12	phenyl	CH	phenyl	CH_2(piperazin-1-yl)
XIA-15	4-F-phenyl	CH	cyclohexyl	CH_2O(tetrahydrofuran-3-yl)
XIA-16	4-F-phenyl	CH	3-cyanophenyl	CH_2O(tetrahydrofuran-3-yl)
XIA-17	4-F-phenyl	CH	2-(2-pyridinyl)ethyl	CH_2O(tetrahydrofuran-3-yl)
XIA-18	4-F-phenyl	CH	1-benzyl-piperidin-4-yl	CH_2O(tetrahydrofuran-3-yl)
XIA-19	4-F-phenyl	CH	4-cyclohexanol	$CH_2OCH_2CH_2OCH_3$
XIA-20	4-F-phenyl	CH	cyclohexyl	$CH_2OCH_2CH_2OCH_3$
XIA-21	4-F-phenyl	CH	2-(2-pyridinyl)ethyl	$CH_2OCH_2CH_2OCH_3$
XIA-22	4-F-phenyl	CH	1-benzyl-piperidin-4-yl	$CH_2OCH_2CH_2OCH_3$
XIA-23	4-F-phenyl	CH	4-cyclohexanol	CH_2(morpholin-4-yl)
XIA-24	4-F-phenyl	CH	cyclohexyl	CH_2(morpholin-4-yl)
XIA-25	4-F-phenyl	CH	3-cyanophenyl	CH_2(morpholin-4-yl)
XIA-26	4-F-phenyl	CH	2-(2-pyridinyl)ethyl	CH_2(morpholin-4-yl)
XIA-27	4-F-phenyl	CH	1-benzyl-piperidin-4-yl	CH_2(morpholin-4-yl)
XIA-28	4-F-phenyl	CH	4-cyclohexanol	CH_2OCH_3
XIA-29	4-F-phenyl	CH	cyclohexyl	CH_2OCH_3
XIA-30	4-F-phenyl	CH	3-cyanophenyl	CH_2OCH_3
XIA-31	4-F-phenyl	CH	2-(2-pyridinyl)ethyl	CH_2OCH_3
XIA-32	4-F-phenyl	CH	1-benzyl-piperidin-4-yl	CH_2OCH_3
XIA-33	4-F-phenyl	CH	4-cyclohexanol	CH_2OCH_3
XIA-34	4-F-phenyl	CH	cyclohexyl	CH_2OCH_3
XIA-35	4-F-phenyl	CH	3-cyanophenyl	CH_2OCH_3
XIA-36	4-F-phenyl	CH	2-(2-pyridinyl)ethyl	CH_2OCH_3
XIA-37	4-F-phenyl	CH	4-cyclohexanol	CH_2O(tetrahydrofuran-3-yl)
XIA-38	4-F-phenyl	CH	cyclohexyl	CH_2O(tetrahydrofuran-3-yl)
XIA-41	4-F-phenyl	CH	4-methoxybenzyl	CH_2OCH_3

(e) a compound selected from:

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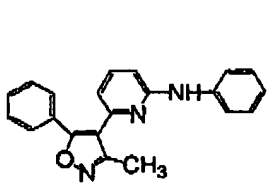
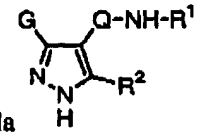
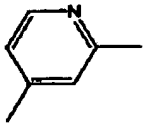


IB-3 or IB-24;

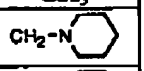
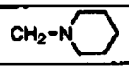


(f) a compound having the formula :



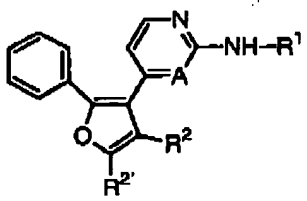
wherein Q is and

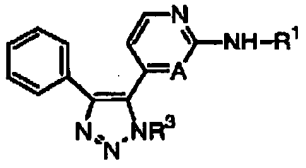
G, R^1 and R^2 are defined as

No.	G	R^1	R^2
IC-1	4-F-phenyl	Phenyl	H
IC-2	4-F-phenyl	Cyclohexyl	H
IC-3	4-F-phenyl	Isoquinolin-4-yl	H
IC-4	4-F-phenyl	6-MeO-naphthalen-2-yl	H
IC-5	4-F-phenyl	4-cyclohexanol	H
IC-9	4-F-phenyl	Cyclohexyl	CH_3
IC-10	4-F-phenyl	Cyclohexyl	
IC-11	Phenyl	Cyclohexyl	

and

(g) a compound of formulae:





:

ID or IE

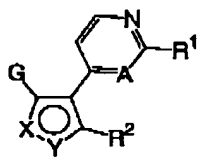
wherein R^1 is phenyl, $R^{2'}$ is hydrogen and A is CH, and

R^2 is H or CH_3 in formula ID; or

R^3 is H or CH_3 in formula IE.

9. (Canceled).

10. (Previously presented) A compound having the formula:



wherein:

X-Y is N-O or O-N;

A is CH;

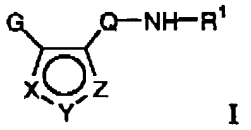
G is R, aryl or substituted aryl;

R is aliphatic or substituted aliphatic;

R^2 is selected from hydrogen, -R, $-CH_2OR$, $-CH_2OH$, -CH=O, $-CH_2SR$, $-CH_2S(O)_2R$, $-CH_2(C=O)R$, $-CH_2CO_2R$, $-CH_2CO_2H$, $-CH_2CN$, $-CH_2NHR$, $-CH_2N(R)_2$, -CH=N-OR, -CH=NNHR, $-CH=NN(R)_2$, -CH=NNHCOR, $-CH=NNHCO_2R$, $-CH=NNHSO_2R$, -aryl, -substituted aryl, $-CH_2$(aryl), $-CH_2$(substituted aryl), $-CH_2NH_2$, $-CH_2NHCOR$, $-CH_2NHCONHR$, $-CH_2NHCON(R)_2$, $-CH_2NRCOR$, $-CH_2NHCO_2R$, $-CH_2CONHR$, $-CH_2CON(R)_2$, $-CH_2SO_2NH_2$, $-CH_2$(heterocyclyl), $-CH_2$(substituted heterocyclyl), -(heterocyclyl), or -(substituted heterocyclyl).

11. (Currently amended) A pharmaceutical composition comprising an amount of a compound according to any one of claims 1-8 effective to inhibit JNK, and a pharmaceutically acceptable carrier.

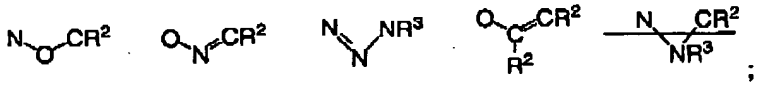
12. (Currently amended) A method for treating rheumatoid arthritis ~~a disease state or condition in mammals that is alleviated by treatment with a protein kinase inhibitor,~~ comprising administering to a mammal in need of ~~such a treatment~~ said treating a therapeutically effective amount of a compound of formula I:



I

wherein:

X-Y-Z is selected from one of the following:



;

R^1 is H, $CONH_2$, $T_{(n)}$-R, or $T_{(n)}$-Ar^2;

R is an aliphatic or substituted aliphatic group;

n is zero or one;

T is C(=O), CO_2, CONH, $S(O)_2$, $S(O)_2NH$, $COCH_2$ or CH_2;

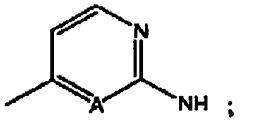
each R^2 is independently selected from hydrogen, -R, $-CH_2OR$, $-CH_2OH$, -CH=O, $-CH_2SR$, $-CH_2S(O)_2R$, $-CH_2(C=O)R$, $-CH_2CO_2R$, $-CH_2CO_2H$, $-CH_2CN$, $-CH_2NHR$, $-CH_2N(R)_2$, -CH=N-OR, -CH=NNHR, $-CH=NN(R)_2$, -CH=NNHCOR, $-CH=NNHCO_2R$, $-CH=NNHSO_2R$, -aryl, -substituted aryl, $-CH_2$(aryl), $-CH_2$(substituted aryl), $-CH_2NH_2$, $-CH_2NHCOR$, $-CH_2NHCONHR$, $-CH_2NHCON(R)_2$, $-CH_2NRCOR$, $-CH_2NHCO_2R$, $-CH_2CONHR$, $-CH_2CON(R)_2$, $-CH_2SO_2NH_2$, $-CH_2$(heterocyclyl), $-CH_2$(substituted heterocyclyl), -(heterocyclyl), or -(substituted heterocyclyl);

each R^3 is independently selected from hydrogen, R, COR, CO_2R or $S(O)_2R$;

G is R or Ar^1;

Ar^1 is aryl, substituted aryl, aralkyl, substituted aralkyl, heterocyclyl, or substituted heterocyclyl, wherein Ar^1 is optionally fused to a partially unsaturated or fully unsaturated five to seven membered ring containing zero to three heteroatoms;

Q-NH is



;

wherein the H of Q-NH is optionally replaced by R^3;

A is CR^3;

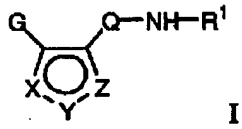
Ar^2 is aryl, substituted aryl, heterocyclyl or substituted heterocyclyl, wherein Ar^2 is optionally fused to a partially unsaturated or fully unsaturated five to seven membered ring containing zero to three heteroatoms;

wherein each substitutable carbon atom in Ar^2, including the fused ring when present, is optionally and independently substituted by halo, R, OR, SR, OH, NO_2, CN, NH_2, NHR, $N(R)_2$, NHCOR, NHCONHR, $NHCON(R)_2$, NRCOR, $NHCO_2R$, CO_2R, CO_2H, COR, CONHR, $CON(R)_2$, $S(O)_2R$, $SONH_2$, S(O)R, SO_2NHR, or $NHS(O)_2R$, and wherein each saturated carbon in the fused ring is further optionally and independently substituted by =O, =S, =NNHR, $=NNR_2$, =N-OR, =NNHCOR, $=NNHCO_2R$, $=NNHSO_2R$, or =NR; and

wherein each substitutable nitrogen atom in Ar^2 is optionally substituted by R, COR, $S(O)_2R$, or CO_2R.

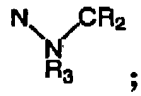
13-24. (Canceled)

25. (New) A compound having the formula



I

wherein:

X-Y-Z is 

;

R^1 is cyclohexyl, cyclohexanol-4-yl, cyclohexanon-4-yl, or an optionally substituted phenyl, naphthyl, pyridyl, quinolinyl, thienyl or indanyl; wherein each substitutable carbon atom of said optionally substituted phenyl, naphthyl, pyridyl, quinolinyl, thienyl or indanyl is optionally and independently substituted by halo, R, OR, SR, OH, NO_2, CN, NH_2, NHR, $N(R)_2$, NHCOR, NHCONHR, $NHCON(R)_2$, NRCOR,

$NHCO_2R$, CO_2R, CO_2H, COR, CONHR, $CON(R)_2$, $S(O)_2R$, $SONH_2$, S(O)R, SO_2NHR, or $NHS(O)_2R$, and wherein each saturated carbon in the fused ring is further optionally and independently substituted by =O, =S, =NNHR, $=NNR_2$, =N-OR, =NNHCOR, $=NNHCO_2R$, $=NNHSO_2R$, or =NR; and wherein each substitutable nitrogen atom of said phenyl, naphthyl, pyridyl, quinolinyl, thienyl or indanyl is optionally substituted by R, COR, $S(O)_2R$, or CO_2R;

R is an aliphatic or substituted aliphatic group;

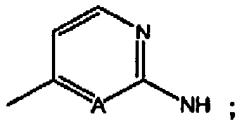
each R^2 is independently selected from hydrogen, -R, $-CH_2OR$, $-CH_2OH$, -CH=O, $-CH_2SR$, $-CH_2S(O)_2R$, $-CH_2(C=O)R$, $-CH_2CO_2R$, $-CH_2CO_2H$, $-CH_2CN$, $-CH_2NHR$, $-CH_2N(R)_2$, -CH=N-OR, -CH=NNHR, $-CH=NN(R)_2$, -CH=NNHCOR, $-CH=NNHCO_2R$, $-CH=NNHSO_2R$, -aryl, -substituted aryl, $-CH_2$(aryl), $-CH_2$(substituted aryl), $-CH_2NH_2$, $-CH_2NHCOR$, $-CH_2NHCONHR$, $-CH_2NHCON(R)_2$, $-CH_2NRCOR$, $-CH_2NHCO_2R$, $-CH_2CONHR$, $-CH_2CON(R)_2$, $-CH_2SO_2NH_2$, $-CH_2$(heterocyclyl), $-CH_2$(substituted heterocyclyl), -(heterocyclyl), or -(substituted heterocyclyl);

each R^3 is independently selected from hydrogen, R, COR, CO_2R or $S(O)_2R$;

G is R or Ar^1;

Ar^1 is aryl, substituted aryl, aralkyl, substituted aralkyl, heterocyclyl, or substituted heterocyclyl, wherein Ar^1 is optionally fused to a partially unsaturated or fully unsaturated five to seven membered ring containing zero to three heteroatoms;

Q-NH is



;

wherein the H of Q-NH is optionally replaced by R^3; and

A is CR^3.

26. (New) A pharmaceutical composition comprising an amount of a compound according to claim 25 effective to inhibit JNK, and a pharmaceutically acceptable carrier.

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Application No.: 10/779,532
Applicants: Green et al.

27. (New) A method for treating rheumatoid arthritis, comprising administering to a mammal in need of such a treatment a therapeutically effective amount of a compound according to claim 25.